INTRODUCTION

High intensity focused ultrasound (HIFU) has been shown to extracorporeally emulsify regions of bulk tissue by shock wave heating and millisecond boiling or by histotripsy [1,2]. The result is a liquefied core of tissue containing submicron-sized pieces with sharply demarcated boundaries between bulk and treated tissues (Figure 1). However, the question persists of how millimeter-sized boiling bubbles or cavitation bubble clouds can produce submicron-sized tissue fragments. We hypothesize that the millimeter-sized bubbles are large enough to act as a pressure release interface, such that a miniature acoustic fountain forms and acoustic atomization occurs at the bubble-tissue interface, fractionating the tissue into submicron-sized fragments.

METHODS/APPROACH

A 2 MHz spherically focused piezoceramic ceramic generating up to 70 MPa peak positive and 15 MPa peak negative pressures was focused at planar and curved interfaces between air and bovine or porcine liver (Figure 2). Exposures of pulse durations between 50 µs and 20 ms and duty factors between 0.0025 and 0.02 were captured with high-speed photography. Pieces ejected from the fountain were collected by suspending a thin, transparent plastic at different distances above the planar fountain and sized using light microscopy. The collected samples were also weighed wet and dry to determine the water content of the projectiles.

RESULTS

Violent removal of fragments less than 30 µm (the size of one pixel) up to 280 µm at velocities of 5-15 m/s with surface displacements up to 2 mm were observed through high-speed filming for all pulsing schemes at maximum transducer amplitudes (Figure 3).

Surface erosion of 1-3 mm diameter was found in less than 10 pulses of 10 ms duration at maximum transducer amplitude in bovine liver (Figure 4). Atomization and surface erosion has been found to be very repeatable (Figure 5). Upon decreasing the transducer amplitude to 15 MPa peak positive and 7 MPa peak negative pressures, atomization became intermittent and no surface erosion was observed.

DISCUSSION/CONCLUSION

Experimental results have thus far supported our hypothesis that tissue is emulsified during millisecond boiling or histotripsy by miniature acoustic fountain formation and acoustic atomization at the bubble-tissue interface. The tissue pieces expelled from the fountain are still slightly larger than those found after millisecond boiling or histotripsy in bulk tissue; however the recirculation of the tissue slurry within the boiling bubble or cavitation bubble cloud may further break down tissue fragments. In addition, the water content of the tissue appears to be of importance in predicting tissue erosion; in a polyacrylamide gel phantom, we see no atomization or surface erosion unless there is a thin film of water on the gel surface. This warrants further study as it may help predict which tissue types can be emulsified using HIFU. Our next steps are to narrow the spatial and temporal focus, looking for the ejection of particles from unstable capillary waves and cavitation bubble collapses, and to analyze tissue viability with histology.

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